



US DEPARTMENT OF DEFENSE

# BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

## Wound Infection

### Blast-related Polytraumatic Extremity Wounds and Infectious Outcomes: Trauma Infectious Disease Outcomes Study (TIDOS)

The Department of Defense (DoD) and Department of Veteran Affairs (VA) Multicenter Cohort Study evaluating Infection-associated Clinical Outcomes in Hospitalized Medical Evacuees following Traumatic Injury (i.e., TIDOS) was initiated on FY09 with the following objectives: 1) Establish a cohort of DoD beneficiaries and active-duty personnel with trauma-related injuries to determine short- and long-term outcomes and potential risk factors associated with infections; 2) Describe the infectious disease epidemiology of trauma-related injuries or other nosocomial infections in the cohort population; 3) Establish a database and bacterial/fungal isolate repository to support future approved sub-studies focused on informing clinical management, disease prevention, or clinical trial design; and 4) Inform DoD efforts to develop real-time tools for combat-related health event/outcome analysis secondary to trauma-related infections during wartime.

The TIDOS project is overseen by the Infectious Disease Clinical Research Program (IDCRP) through the Uniformed Services University of the Health Sciences (USUHS). It is a collaborative project that involves investigators from a variety of disciplines (e.g., infectious disease, trauma surgery, orthopedics, epidemiology, microbiology, pathology, statistics, and molecular biology) across multiple clinical sites, including USUHS, Walter Reed National Military Medical Center (WRNMMC), San Antonio Military Medical Center, Landstuhl Regional Medical Center (LRMC), and the Saint Louis VA Medical Center. In addition, TIDOS also involves collaborations with investigators from US Army Institute of Surgical Research (USAISR), Walter Reed Army Institute of Research (WRAIR), Naval Medical Research Center (NMRC), and the United Kingdom Ministry of Defence Wound Infections Surveillance Programme. The inclusion criteria for the TIDOS project included being an active duty personnel or DoD beneficiary, over 18 years of age, and sustaining a wound or injury during deployment requiring return via LRMC to a participating military hospital in the US. Patient trauma history, ISS, and surgical management was obtained for all military trauma patients (June 2009 through December 2014) through selected data elements retrieved from the DoD Trauma Registry (DoDTR). An infectious diseases module to augment the DoDTR was developed to capture infection-specific data throughout levels of care at participating hospitals. This infectious disease-specific information included diagnoses, treatments (antibiotic usage), and outcomes of bloodstream infections, clinical sepsis, bone and joint infections, skin and soft tissue infections, CNS infections, intra-thoracic/pulmonary infections, and intra-abdominal infection. Prior to hospital discharge, patients were given the opportunity to enroll in the longitudinal TIDOS cohort, which collected long-term infection-related information from patients at pre-determined intervals after hospital discharge (e.g., one month, three months, six months, 12 months, 18 months, and 24 months and then yearly). Information on infectious disease events related to the initial trauma was collected through in-person and telephonic interviews, interaction with health providers, medical record review, and query of electronic healthcare databases. Enrolled patients who entered VA care were also given the opportunity to consent to data abstraction through review of the VA's Compensation and Pension Records Interchange.

Overall, the TIDOS project is one of the largest cohorts of Operation Iraqi Freedom (OIF)/Operation Enduring Freedom (OEF) trauma patients capturing information following injury with an extended follow-up duration, allowing for comprehensive assessment of the full impact of trauma-related infections on military personnel. While there are





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similarities with other populations, wounded military personnel examined in TIDOS sustained trauma with a greater severity than seen in civilian trauma. In particular, patients in TIDOS frequently sustained dismantled blast trauma, resulting in at least one traumatic amputation of a lower extremity, as well as other grievous injuries. The severity of these injuries and inclusive nature of TIDOS makes this cohort unique and of critical relevance to the Military Health System (MHS).

Data gathered through TIDOS was crucial when faced with the emergent outbreak of invasive fungal infections (IFIs) in 2009-10 among patients with blast trauma. Analysis of data obtained through TIDOS identified risk factors for the development of IFIs, assessed clinical outcomes and morbidity (e.g., time to wound closure and amputations/ amputation revisions), examined diagnostic methods, and evaluated wound microbiology. These data supported the development (and refinement) of a Clinical Practice Guideline (CPG) specific to IFI management.<sup>1</sup> Furthermore, as TIDOS collected data through multiple levels of care and maintains a microbiological repository of isolates, the potential transmission of healthcare-associated multidrug-resistant organisms, including ESKAPE pathogens (encompass the six pathogens with growing multidrug resistant virulence: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter*, *Pseudomonas aeruginosa* and *Enterobacter*), is the focus of multiple investigations. Data collected through TIDOS also allowed for the development of CPGs and recommendations related to the prevention of combat trauma-related infections in these wounded Service Members.<sup>2</sup> Lastly, information collected through TIDOS is being utilized for the examination of antimicrobial practice patterns related to adherence to CGPs and potential improvements in antibiotic stewardship. In 2016, research conducted by TIDOS investigators has resulted in seven manuscripts in peer reviewed publications<sup>3,4,5,6,7,8,9</sup> and multiple abstract

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- 3 Tribble, D. R., Li, P., Warkentien, T. E., Lloyd, B. A., Schnaubelt, E. R., Ganesan, A., ... Murray, C. K. (2016). Impact of Operational Theater on Combat and Noncombat Trauma-Related Infections. *Military Medicine*, 181(10), 1258–1268. <https://doi.org/10.7205/MILMED-D-15-00368>
- 4 Lewandowski, L. R., Weintrob, A. C., Tribble, D. R., Rodriguez, C. J., Petfield, J., Lloyd, B. A., ... Potter, B. K. (2016). Early Complications and Outcomes in Combat Injury-Related Invasive Fungal Wound Infections: A Case-Control Analysis. *Journal of Orthopaedic Trauma*, 30(3), e93-99. <https://doi.org/10.1097/BOT.0000000000000447>
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- 6 White, B. K., Mende, K., Weintrob, A. C., Beckius, M. L., Zera, W. C., Lu, D., ... Murray, C. K. (2016). Epidemiology and antimicrobial susceptibilities of wound isolates of obligate anaerobes from combat casualties. *Diagnostic Microbiology and Infectious Disease*, 84(2), 144–150. <https://doi.org/10.1016/j.diagmicrobio.2015.10.010>
- 7 Lewis, J. D., Wassermann, E. M., Chao, W., Ramage, A. E., Robin, D. A., & Clauw, D. J. (2012). Central sensitization as a component of post-deployment syndrome. *NeuroRehabilitation*, 31(4), 367–372. <https://doi.org/10.3233/NRE-2012-00805>
- 8 Heaton, S. M., Weintrob, A. C., Downing, K., Keenan, B., Aggarwal, D., Shaikh, F., ... Wells, J. (2016). Histopathological techniques for the diagnosis of combat-related invasive fungal wound infections. *BMC Clinical Pathology*, 16, 11. <https://doi.org/10.1186/s12907-016-0033-9>
- 9 Mende, K., Beckius, M. L., Zera, W. C., Yu, X., Li, P., Tribble, D. R., & Murray, C. K. (2016). Lack of doxycycline antimalarial prophylaxis impact on *Staphylococcus aureus* tetracycline resistance. *Diagnostic Microbiology and Infectious Disease*, 86(2), 211–220. <https://doi.org/10.1016/j.diagmicrobio.2016.07.014>





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presentations at national and international meetings.<sup>10,11,12</sup>

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- 10 Mangum, L. C., Garcia, G. R., & Tribble, D. R. (2016). Biofilm Formation Capacity among *Acinetobacter baumannii* and *Enterococcus* species isolates from Clinical Wound Infections of Injured U.S. Military Personnel. Presented at the Military Health System Research Symposium, Kissimmee, FL.
  - 11 Heitkamp, R., Li, P., & Mende, K. (2016). *Enterococcus* spp. in Extremity Trauma Wounds. Presented at the Military Health System Research Symposium, Kissimmee, FL.
  - 12 Tribble, D. R. (2016). The U.S. Department of Defense Trauma Infectious Disease Outcomes Study (TIDOS). Presented at the 3rd Force Health Protection Congress, Hamburg, Germany.

